PATENT COOPERATION TREATY

DOCKETED
SEP 18 2001

PCT

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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Subject to PTA? ~~YES~~/NO
per ~~docket~~/ECB)
mm 09/12/01

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	06.09.2001
Applicant's or agent's file reference I0308/7000WO	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/25877	21/09/2000	21/09/1999

International Patent Classification (IPC) or both national classification and IPC
C12N15/67

Applicant
ISIS INNOVATION LIMITED et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 21/01/2002.

Name and mailing address of the international preliminary examining authority:
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I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-37 as originally filed

Claims, No.:

1-31 as originally filed

Drawings, sheets:

1/3-3/3 as originally filed

Sequence listing part of the description, pages:

1-8, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:
   see separate sheet

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	
Inventive step (IS)	Claims	16-18, 20-23, 29-31; NO
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D1: WO 95 05481 A (ISIS INNOVATION ;COOKSON WILLIAM OSMOND CHARLES (GB); HOPKIN JULIA) 23 February 1995 (1995-02-23)

D2: US-A-5 807 988 (JOUVIN MARIE-HELENE ET AL) 15 September 1998 (1998-09-15)

Re Item IV

Lack of unity of invention

The following groups of inventions have been identified:

i) a method for inhibiting expression of an FcεRI receptor or of an FcεRIα chain in a cell or in a subject (claims 1-7, 8-15, 24-28)

ii) a method of screening for agents modulating FcεRI receptor expression (claims 16-20)

iii) a method of screening for agents modulating FcεRIβ chain variant expression (claims 21-23)

iv) a method for determining whether a subject has a condition mediated by IgE (claims 29-31)

According to Rule 13 PCT, an application must relate only to one invention or to a group of inventions so linked as to form a single inventive concept, i.e. having at least one common technical feature defining a contribution over the known prior art. In the present case, the common technical feature among the different identified groups of inventions seems to be an "FcεRIβ chain variant". This feature was already well-known (see document D1). Thus, in the absence of technical feature over the prior art, the IPEA fails to see a common inventive concept among these different groups.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The present application discloses FcεRIβT, an alternative splice variant of the beta subunit of the FcεRI receptor. This variant causes a decrease in surface expression of the FcεRI receptor, in particular of its alpha subunit (FcεRIα). Since FcεRIβT is unstable, the negative regulation of cell surface expression of FcεRIα is potentially caused by turnover of nascent receptor complexes.

Inventive step (Art. 33(3) PCT)

Claims 16-18, 20-23 and 29-31 lack an inventive step in view of D1 and D2.

D2 teaches the detection of candidate substances inhibiting the formation or function of FcεRI: upon incubation of cells with a candidate inhibitor, receptor activity is determined and is compared to the receptor activity of cells in the absence of the assayed candidate substance (example 11, column 23). The subject-matter of claims 16 and 21 relates to the same method, using different control cells ("contacted with an FcεRIβ chain variant"), respectively screening for substances modulating expression of an FcεRIβ chain variant. FcεRIβ chain variants associated with IgE-mediated hypersensitivity are known from D1. Claims 16 and 21 are considered to be directed to the use of a known technique in a closely analogous situation and do not involve a new technical effect over the prior art. Therefore the subject-matter of said claims is considered to lack an inventive contribution.

D1 discloses a method of diagnosing atopy or a predisposition to atopy in an individual, this method comprising demonstrating the presence in the individual of a β chain variant of the FcεRI receptor (D1, claim1). Claim 29 relates to the same method in an analogous situation, since the difference merely resides in the fact that lower levels and not elevated levels of FcεRIβ chain variant are indicative for the predisposition of the subject to atopy. Claim 29 is thus considered to lack an inventive step.

Dependant claims 17, 18, 20, 22, 23, 30 and 31 do not appear to contain any additional features involving an inventive step.

Re Item VIII

Certain observations on the international application

Clarity of the claims (Art. 6 PCT)

1. The following terms are unclear and render the scope of the corresponding claims broader than justified by the description:

a. "FcεRIβ chain variant" (all claims), since only one specific variant, FcεRIβT, is disclosed in the present application. This term however refers to all possible modifications of the wild-type FcεRIβ chain.

b. "contacting" (claims 1, 6-7, 16, 21, 24, 27-28), because the description only gives support for transfection of the FcεRIβT chain variant into the cells.

c. "inhibits expression" (claims 1, 2, 4, 11, 13, 24, 25), since a FcεRIβ chain variant inhibiting replication, transcription and/or translation of FcεRI receptor genes

(description page 7) is not disclosed.
d. "modulating agent" (claim 16), because the claimed screening method only involves assaying for an inhibitory agent (description pages 13-14).

2. The term "effective amount" (claims 1, 8, 24) is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear.

3. The scope of claims 1, 8, 24 is unclear, since their subject-matter is defined in terms of a result to be achieved ("to inhibit expression") and not in terms of technical features of the claimed invention (Preliminary Examination Guidelines, III-4.7.).

4. Claim 15 lacks support from the description, since an anti-allergic agent which can be co-administered in accordance with the claimed invention is not disclosed.

5. The attention of the applicant is drawn to the fact that the subject-matter of claims 7, 8-15 and 28 is directed to methods of treatment of the human or animal body by therapy and thus, it may be excluded from examination by Article 34(4)(a)(i) PCT in combination with Rule 67(iv)PCT. The same remark applies to the subject-matter of claims 29-31, as far as it concerns diagnostic methods practised on the human or animal body.
For such a subject-matter no unified criteria exist in the PCT Contracting States for the assessment whether it is industrially applicable or not. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.